REMARKS

Claims 20-30, and 55-59 are pending in the present application.

CLAIM REJECTIONS

In the Office Action of January 3, 2005 (hereafter "Office Action") the Examiner rejected:

I) claims 20-30 under 35 U.S.C. §103(a) as being unpatentable over Huber et al., (US 5,219,764) (hereafter "Huber") in view of Pandori et al., (Chemistry & Biology Vol. 9, 567-573) (hereafter "Pandori") and

II) claims 20-30 under 35 U.S.C . §112, first paragraph, as failing to comply with the written description requirement.

I. The Claims Are Not Obvious

The Examiner has rejected claims 20-30 under 35 U.S.C. §103(a) as being unpatentable over Huber et al., (US 5,219,764) (hereafter "Huber") in view of Pandori et al., (Chemistry & Biology Vol. 9, 567-573) (hereafter "Pandori").

Applicants respectfully submit that the Examiner has not provided how Huber alone or in view of Pandori teaches, motives or suggests the elements of these rejected claims. The Examiner is improperly using the Applicants' Specification to reconstruct, in hindsight, the invention as claimed. However, without acquiescing to the Examiner's rejections, but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended claims 20, 24, 28, and 30, and added new claims 55-59 to further define embodiments.

Detection of heavy atom isotopes are taught by neither Huber nor Pandori

The Examiner primarily argues that the currently claimed compounds and the compounds disclosed in Huber and Pandori are similar in structure, and therefore the claimed compounds are obvious. Respectfully, we disagree. However, without acquiescing to the Examiner's rejections, but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended independent claims 20, 24, 28 and 30 to further emphasize the embodiments encompassed by heavy atom isotopes.

The Examiner states that "[t]he motivation to make the claimed compounds derived from the expectation the structurally similar compounds would possess similar activity, (i.e. pharmacological use)" Office Action Dated November 2, 2005, page 6, second paragraph. However, simply because compounds may have some similar structural aspects, that does not necessary render the claimed compounds obvious. See In re Ochiai, 71 F.3d 1565 (Fed. Cir. 1995) (overruling an obviousness rejection on the assertion that the starting materials recited in disputed claims were "similar" to those of the prior art) and In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995).

> [I]n making the assessment of differences between the prior art and the claimed subject matter, section 103 specifically requires consideration of the claimed invention "as a whole." Inventions typically are new combinations of existing principles or features. Envtl. Designs, Ltd. v. Union Oil Co., 713 F.2d 693, 698 (Fed. Cir. 1983) (noting that "virtually all [inventions] are combinations of old elements"). The "as a whole" instruction in title 35 prevents evaluation of the invention part by part. [Ruiz v. A.B. Chance Co., 357 F.3d 1270, 1275 (Fed. Cir. 2004)]. Without this important requirement, an obviousness assessment might successfully break an invention into its component parts, then find a prior art reference corresponding to each component. Id. This line of reasoning would import hindsight into the obviousness determination by using the invention as a roadmap to find its prior art components. Further, this improper method would discount **the value of combining various existing features or principles in a new way to achieve a new result - often the essence of invention**. Princeton Biochemicals v. Beckman Coulter (Fed. Cir. 2005) (emphasis added).

<u>The "New Way" to achieve "New Superior Results"</u>

Here, the use of the compounds with heavy atom isotopes enables the Applicants to utilized a superior method of detecting mixtures of the photocleaved products by mass spectroscopy with the techniques disclosed in the specification. Neither Huber nor Pandori suggests identifying components from a mixture using the claimed compositions. Neither Huber nor Pandori render the claimed compounds obvious.

II. The Claims Are Not Indefinite

The Examiner argues that "Claims 20-30 fail to meet the written description requirement" of 35 U.S.C. Section 112, first paragraph because the terms "PRG," "protein reactive group," "isotopes," "sulfhydryl reactive group," "amine reactive group," and "aliphatic hydrocarbon chain," are not described in the specification. The Examiner mentions that "[a]pplicant is invited to point out where in the original specification, claims or drawing the terms are defined." Office Action Dated November 2, 2005, page 7, last paragraph. The exact allegations of the rejection by the Examiner are unclear, and the Applicants request further elaboration. However, in order to further prosecution, we are assuming that the Examiner is arguing either 1) that that claims terms must be defined in the specification to meet the written description requirement or 2) that the claim terms are not understandable to one skilled in the art. In either case, we disagree.

First, there is no requirement that a claim term must be expressly defined in the specification in order to meet the written description requirement. See <u>Phillips v. AWH Industries</u>, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*) (". . .requiring that any definition of claim language in the specification be express, is inconsistent with our rulings. . ."). The words of a claim are generally given their ordinary and customary meaning, i.e., the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention. The "ordinary meaning" of a claim term is its meaning to the ordinary artisan after reading the entire patent. <u>Id.</u>

Second, a claim is indefinite if, when read in light of specification, the claim does not reasonably apprise those skilled in the art of the scope of the invention. <u>Howmedica Osteonics v. Tranquil Prospects</u> (Fed Cir 2005). When a claim "is not insolubly ambiguous, it is not invalid

for indefiniteness." Bancorp v. Hartford Life, 359 F.3d 1367, 1372 (Fed. Cir. 2004). With regard to the term "aliphatic hydrocarbon chain," the applicants believe that the term is definite to a person of ordinary skill in the art in question. This is not an unusual term. Indeed, this is a term common to college chemistry texts such as Masterton & Slowinski "Chemical Principles" 2nd Edition, Press of W.B. Saunders Company, page 277 first paragraph and page 616 second paragraph (1969). Moreover, Figure 14B describes the synthesis of an embodiment of the claimed compositions wherein R is an aliphatic hydrocarbon chain.

In the present case, the specification provides that the term "PRG is [that is, it means] the protein reactive group that reacts with functional groups on proteins." See corresponding U.S. Published Application No. 2005/0085630, paragraph 0012, first sentence. In the body of the specification, pages and pages of examples are given (along with tables such as Table 4), indicating that protein reactive groups can be reactive with thiol groups and amino groups (see corresponding U.S. Published Application No. 2005/0085630 paragraphs 0302-0324). Moreover, Figure 14E provides a number of examples of "protein reactive groups," however the Applicants do not intend that the terms be limited to the examples. For example, a "maleimide," which is a "protein reactive group," reacts with proteins containing sulfhydryls, i.e., also a "sulfhydryl reactive group," as suggested by the entry of row 1, column 2 of Figure 14E. In another example, an "NHS ester," which is a "protein reactive group," reacts with proteins containing amines, i.e., also an "amine reactive group," as suggest by the entry of row 3, column 2 of Figure 14E. New claims 55-57 have been added to emphasize these embodiments.

CONCLUSION

Applicants respectfully request that the Examiner's rejections under 35 U.S.C. §§103 and 112 be withdrawn, that claims 20-30, and 55-57 be allowed, and a timely notice of allowance be issued in this case. Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned at 617.984.0616.

Respectfully submitted,

Dated: February 2, 2006

By: ______________________

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The area

this topic deals with solubility in the liquid state and is subdivided according to whether the solute is a liquid, a gas, or a solid.

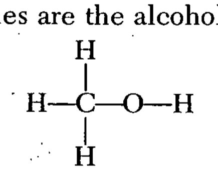
Liquid-Liquid

In discussing the solubility of two liquids in each other, it is sometimes stated that "like dissolves like." A more meaningful way of expressing this same idea is to say that substances that have similar molecular structures and, consequently, intermolecular forces of about the same magnitude will be soluble in each other in all proportions. An illustration of this rule is furnished by the liquid aliphatic hydrocarbons, of general formula C_nH_{2n+2} (C_5H_{12}, C_6H_{14} . . . $C_{18}H_{38}$), all of which are completely miscible with each other. Molecules of these nonpolar substances are held together by dispersion forces which increase only slightly with molecular size. The forces between C_5H_{12} molecules in pure liquid pentane are very nearly the same as those between C_5H_{12} and C_8H_{18} molecules in a solution of pentane in octane. A pentane molecule readily passes into solution in octane because it undergoes virtually no change in environment in the solution process.

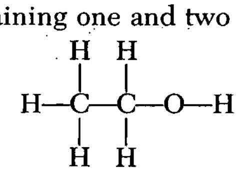
Moderate differences in polarity between solute and solvent seem to have little effect on solubility. Aliphatic hydrocarbons of the type just discussed are as soluble in chloroform ($CHCl_3$, dipole moment = 1.15 Debye units) as they are in each other or in carbon tetrachloride (CCl_4, dipole moment = 0). This reflects the weakness of dipole forces, which make only a minor contribution to the total attractive force between $CHCl_3$ molecules. The fact that the heats of vaporization and surface tensions of chloroform and carbon tetrachloride are almost identical implies that the intermolecular forces in $CHCl_3$ and CCl_4 are nearly the same. It is about as easy to "break into" the liquid structure of $CHCl_3$ as it is with CCl_4, and consequently the two liquids show similar solvent properties despite a considerable difference in polarity.

If one attempts to dissolve a hydrocarbon in water, the situation is quite different. In order to dissolve appreciable quantities of, let us say, pentane in water, one would have to break the strong intermolecular hydrogen bonds holding water molecules together. The large amount of energy required to do this would not be restored in any step of the solution process; the attractive forces in solution between C_5H_{12} and H_2O molecules are probably weaker than those between C_5H_{12} molecules in liquid pentane. Consequently, pentane and other hydrocarbons are only very slightly soluble in water; at 25°C the mole fraction of pentane in a saturated water solution is 0.00003. It is commonly supposed that the few molecules of pentane that dissolve do so by fitting, with minimum distortion, into "holes" in the hydrogen-bonded water structure. This is suggested by the fact that the heats of solution per mole of most liquid hydrocarbons in water are very nearly zero.

Of the relatively few organic liquids which dissolve readily in water, the majority are oxygen-containing compounds of low molecular weight. Two familiar examples are the alcohols containing one and two carbon atoms,



Methyl alcohol



Ethyl alcohol

to rate the scientific areas of progress in this century which have contributed most to the well-being of mankind, it would be only fair to rank our ability to treat illness with medicines obtained through the knowledge of organic chemistry at the top of the list.

24.1 KINDS OF ORGANIC SUBSTANCES

We have pointed out that organic chemistry owes its existence to unique properties of the carbon atom. You will recall that the electron configuration of carbon, $1s^2 2s^2 2p^2$, gives the atom four valence electrons. Through hybridization, or by the principle that electron pairs in a molecule occur at maximum distances from one another, the carbon atom can form four equivalent, strong, covalent bonds, located tetrahedrally about the carbon atom. Of special significance is the fact that bonds between carbon atoms are strong, making for the possibility of long carbon chains in organic molecules. Silicon and germanium, of the same family as carbon, can also form four bonds, but the relative weakness of the Si—Si and Ge—Ge bonds restricts the chemistry of those elements severely. Because the electronegativity of carbon is near that of hydrogen and other nonmetals, such as oxygen, nitrogen, and sulfur, that commonly occur in organic compounds, the bonding in organic compounds is typically covalent in character. Organic substances are therefore primarily molecular, with physical properties determined by molecular interactions due to dispersion forces, dipole forces, or hydrogen bonding.

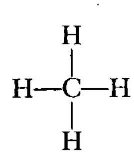
Organic compounds can be classified into groups and subgroups, according to the nature of the covalent bonds and the kinds of atoms present. One very large group includes those substances whose molecules contain only carbon and hydrogen atoms. These substances are called **hydrocarbons**, and, depending on the kinds of carbon bonds present, they can be further classified as paraffins, olefins, acetylenes, or aromatic substances. In this section we will first consider the hydrocarbons, then some compounds containing halogens, and finally oxygen-containing organic compounds.

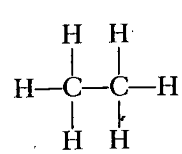
Organic chemistry is the chemistry of hydrocarbons and their derivatives.

Saturated Hydrocarbons: Paraffins and Cycloparaffins

One large and structurally simple subgroup of the hydrocarbons includes those substances whose molecules contain only single carbon-carbon bonds. These substances are called **saturated** hydrocarbons or **paraffins**. In the paraffins the carbon atoms are bonded to each other in chains, which may be long or short, single or branched. In some cases the ends of a chain are bonded to each other, and **cycloparaffins** result.

The simplest paraffinic substances are methane, CH_4, and ethane, C_2H_6, whose molecules we used as models in the discussion of covalent bonding in Chapter 8.


Methane


Ethane